amended claim recitations. For instance, one skilled in the art would have known that the phrase "a single stranded nucleic acid molecule" in the preamble of claim 42 as filed was intended to be "a single stranded DNA molecule" because the phrase "the single stranded DNA molecule" was recited several times throughout the body of claim 42 and "single stranded nucleic acid molecule" was never recited in the body of claim 42. Also, in claim 48, it was apparent to one skilled in the art that "the double stranded DNA molecule" in claim 48 as filed actually was meant to be "the single stranded DNA molecule" because "single stranded DNA molecule" was recited several times in the body of claim 42, upon which claim 48 depends.

The amendments to the Specification have been made to provide a proper Brief Description of the Drawings in which each panel, e.g. Fig. 1A, Fig. 1B, etc., of the drawings is described.

Drawings

The Office Action Summary states that the Drawings were objected to. Applicants believe that the amendment to the Specification with a proper Brief Description of the Drawings section has rendered the objection to the drawings moot.

Claim Rejections -- 35 U.S.C. 112, Second Paragraph

Claim 41 was rejected because "the primer" lacked proper antecedent basis. The term "the primer" has been replaced with "the two primers" which has proper antecedent basis.

Claims 42-49 were rejected because "the single stranded DNA molecule" in claim 42, line 3, lacked proper antecedent basis. The preamble of claim 42 has been amended to refer to "a single stranded DNA molecule" to provide proper antecedent basis to "the single stranded DNA molecule" recited in the body of claim 42.

Claim 48 was rejected because "the double stranded DNA molecule" lacked proper antecedent basis. Claim 48 has been amended to recite "the single stranded DNA molecule" according to proper antecedent basis.

Withdrawal of the indefinite rejections is requested.

Obviousness Type Double Patenting

Claims 34-58 were rejected for provisional obviousness double patenting over claims 1-62 of US Pat. No. 6,225,092 (hereinafter referred to as US '092), which issued from the grandparent application, No. 08/991,184. Applicants respectfully traverse the rejection, but a Terminal Disclaimer attached has rendered the rejection moot.

Claims 34-58 of this application are patentably distinct from claims 1-62 of US '092. Claims 34-58 of this application are broader in scope than claims 1-62 of US '092. Applicants submit that claims 34-58, drawn to a genus, fail to render obvious the species according to claims 1-62 of US '092 because there would have been no guidance in the art to lead a person of ordinary skill in the art from the genus of claims 34-58 to reach the species of claims 1-62 of US '092. Based on the genus of claims 34-56, the person would have no motivation to use the specific ratio of an amount of the second thermostable DNA polymerase to an amount of the first thermostable DNA polymerase to be 1:X, wherein X is at least 16, as recited in claim 1 of US '092. Thus,

claims 1-62 of US '092 are patentably distinct from claims 34-56 of the instant application.

Withdrawal of the obviousness type double patenting rejection is requested.

Claim Rejection -- 35 U.S.C. 102

Claims 34-58 were rejected under 35 U.S.C. § 102(e) as anticipated by Koster et al. (U.S. Patent No. 5,928,906, hereinafter referred to as US '906).

Applicants respectfully traverse the rejection of claims 34-58 on the ground that '906 is non-enabled as shown by a Declaration (a copy is attached) filed during the prosecution of the grandparent application (Serial No. 08/991,184). To be relied upon in a proper anticipatory rejection, a prior art reference must be enabling in combination with the knowledge of a person of ordinary skill in the art. See *In re Donohue*, 226 USPQ 619 (Fed. Cir. 1985); *In re Hoeksema*, 158 USPQ 596 (CCPA 1968). The Declaration by Dr. Christian Kilger, executed on February 28, 2000, presents experimental evidence to show that the disclosure of US '906 fails to teach a person skilled in the art how to practice the method of US '906 unless the person performs undue experimentation. Since a method of simultaneous amplification and sequencing of a nucleic acid was not known to the person skilled in the art before the PCT application for the instant application was published, the knowledge of the person would not be sufficient to supplement the teachings of US '906 to allow the person to practice the method of US '906 unless undue experimentation is performed by the person. Thus, US '906 failed to put in the possession of the public the method of simultaneous amplification and sequencing of the nucleic acid molecule. Since US '906 does not

qualify as a valid prior art reference, withdrawal of the anticipatory rejection is requested.

Conclusion

In view of the amendment and the above reasoning, applicants submit that the application is in a condition for allowance. A Notice of Allowance is believed in order.

In the event that the filing of this paper is not deemed timely, applicants petition for an appropriate extension of time. Any petition fee for the extension of time and any other fees that may be required in relation to this paper can be charged to Deposit Account No. 01-2300, referencing Docket No. 101614-00009.

Respectfully submitted,

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Enclosures: Appendix
Declaration
Terminal Disclaimer
Petition for Extension of Time

KLW:elp

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APPENDIX

MARKED UP VERSION OF THE AMENDMENT

In the Specification:

Page 13, line 15, delete "Short description of the figures" and insert therefor --Brief Description of the Drawings--.

Page 13, please replace the 4th full paragraph with the following:

[Fig. 1.] Figs. 1A and 1B. Schematic representation of the method of the present invention (DEXTAQ). A first polymerase of the present invention [(A)] Fig. 1A which carries a "Tabor-Richardson" mutation for discriminating towards ddNTPs preferentially incorporates ddNTPs and produces the sequence ladder. A second polymerase of the present invention which, compared to the said first thermostable DNA polymerase [(B)] Fig. 1B, has a reduced ability to incorporate dideoxynucleotides, preferably incorporates dNTPs and mainly produces products of full length and provides the uncoupled, direct, exponential amplification and sequence reaction with additional sequencing templates.

Please replace the paragraphs beginning on page 13, line 24 and page 14, line 5 with the following combined paragraph:

[Fig. 2] Figs. 2A-2F. 60 ng of total genomic DNA was subjected to a direct, uncoupled sequencing reaction using 6 pmol of an FITC-labelled primer (CCR5-2) and 3 pmol of an unlabelled primer (CCR5-1). The section shown in all [windows] figure panels is only at a distance of 20 base pairs from the end of the template and the last bases are part

of the primer that generates the second template. No additional Taq DNA polymerase was added to the reaction that is shown in [window A] Fig. 2A. Increasing amounts of Taq DNA polymerase were added to the reactions that are shown in [window B] Fig. 2B (0.25 units), [C] Fig. 2C (0.5 units), [D] Fig. 2D (1.0 units) and [E] Fig. 2E (2.0 units). In cases where no Taq DNA polymerase had been added, the A.L.F. software was not able to process a sequence. A better ratio between signal and noise is seen in the cases in which Taq DNA polymerase had been added. [Fig. 2A.] In Fig. 2F, 60 ng of total genomic DNA was subjected to an uncoupled, direct amplification and sequencing reaction using equimolar amounts i.e. 3 pmol each of an FITC-labelled primer (CCR5-2) and of an unlabelled primer (CCR5-1). The A.L.F. software was able to process 290 bases. The reactions were carried out using 0.25 units Taq DNA polymerase and standard ThermoSequenase reagents.

Please replace the paragraph on page 14, lines 11-18 with the following:

[Fig. 3.] Figs. 3A-3C. An uncoupled, direct, exponential amplification and sequencing reaction was carried out in combination with various thermostable polymerases which do not carry the "Tabor-Richardson" mutation. [Window A] Fig. 3A shows a reaction in which 2.5 units Klentaq polymerase were added to a direct, uncoupled amplification and sequencing reaction which was carried out with 60 ng total genomic DNA. [Window B] Fig. 3B shows a direct, uncoupled, exponential amplification and sequencing reaction which was carried out with standard Taq DNA polymerase and [window C] Fig. 3C shows a reaction in which 0.25 units Tth polymerase was added.

In the Claims:

41. (Amended) A process of claim 34, wherein the two primers are [primer is] mobility modified and the amplified and chain terminated fragments are detected by electrophoresis.

42. (Amended) A process for simultaneously amplifying and sequencing a single stranded [nucleic acid] DNA molecule, comprising the steps of:

a) contacting the single stranded DNA molecule with: (i) a primer that can hybridize to the single stranded DNA molecule, (ii) a set of chain elongating nucleotides, (iii) at least one chain terminating nucleotide, (iv) a first DNA polymerase; and (v) a second DNA polymerase, which has a higher affinity towards the chain terminating nucleotide relative to the first polymerase, so that polymerization by the first polymerase results in amplification and polymerization by the second polymerase results in the formation of chain terminated fragments;

b) detecting the chain terminated fragments by a detection means; and

c) aligning the fragments to determine the sequence of the single stranded nucleic acid molecule.

48. (Amended) A process of claim 42, wherein the single [double] stranded DNA molecule has been synthesized from RNA using a reverse transcriptase.